Eli Lilly and Company
Lilly Corporate Center
Indianapolis, Indiana 46285
U.S.A.

December 2, 2002

Dear Doctor:

As you may be aware, Eli Lilly and Company recently discontinued production of injectable Vancocin® HCl (sterile vancomycin hydrochloride, USP) in the United States. Injectable vancomycin products continue to be manufactured and sold in the United States by Abbott Laboratories, American Pharmaceutical Partners (APP), and Baxter Healthcare Corporation. The Food and Drug Administration (FDA) has approved these products as therapeutically equivalent to Vancocin. Lilly has supplied and will continue to supply Baxter with vancomycin for manufacture of their pre-mixed injectable products (500 mg per 100 mL and 1 gram per 200 mL).

Despite the availability of several forms of intravenous vancomycin, some physicians continue to prefer Vancocin for intraperitoneal administration to treat systemic infections caused by susceptible organisms in patients undergoing continuous ambulatory peritoneal dialysis (CAPD). This may be due to concerns about cases of chemical peritonitis following intraperitoneal administration of vancomycin that were reported in the literature in the late 1980s. Although the exact cause of the chemical peritonitis was never determined, we are not aware of any evidence that suggests that intraperitoneal administration of *currently* available forms of vancomycin is more likely to cause peritonitis than Vancocin. It should be noted that the safety and efficacy of vancomycin administered by intraperitoneal infusion has not been systematically evaluated and is considered by FDA to be an unapproved use. *(Please see accompanying Prescribing Information.)*

To assist physicians who may be concerned about switching from Vancocin to other injectable vancomycin products for CAPD patients, Lilly has worked with the FDA to set up an allocation program to provide access to a limited supply from the remaining inventory of Vancocin 1 gram vials. Enrollment is limited to physicians treating CAPD patients who are considered to be at significant risk for chemical peritonitis *and* unable to use alternative products, including the Baxter products.

Please call 1-800-LILLYRX between 8:00 am and 7:00 pm, EST, Monday through Friday, for more details on the program and eligibility criteria. If eligibility criteria are met you will be provided additional information concerning the program and how to obtain a limited supply of Vancocin.

Sincerely,

Donald G. Therasse, M.D.
Executive Director
US Medical Division
Lilly Research Laboratories
Eli Lilly and Company

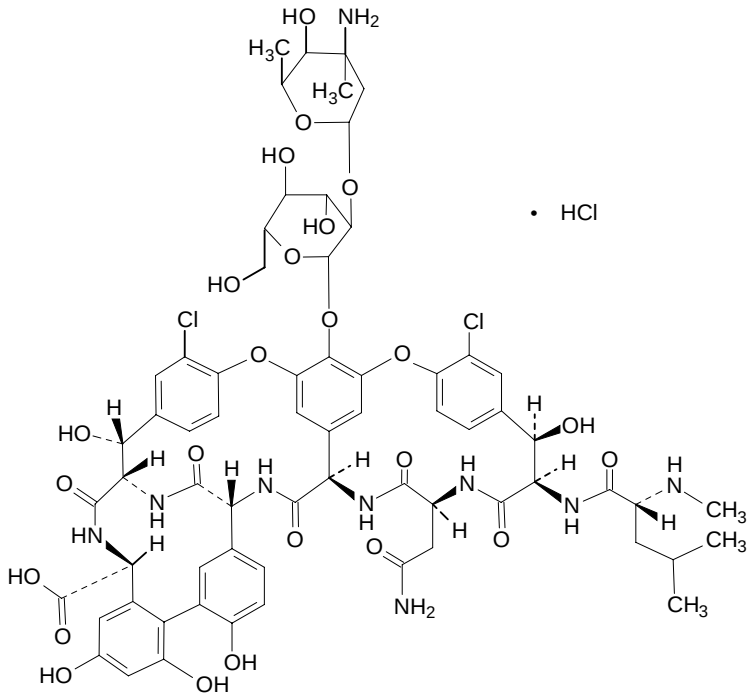
PA 1858 AMP

VIALS
VANCOCIN® HCl
STERILE VANCOMYCIN HYDROCHLORIDE, USP
INTRA**V**ENOUS

DESCRIPTION

Vancocin® HCl (Sterile Vancomycin Hydrochloride, USP), IntraVenous, is a chromatographically purified, tricyclic glycopeptide antibiotic derived from *Amycolatopsis orientalis* (formerly *Nocardia orientalis*) and has the chemical formula $C_{66}H_{75}Cl_2N_9O_{24}$•HCl. The molecular weight is 1,485.73; 500 mg of the base is equivalent to 0.34 mmol.

Vancomycin hydrochloride has the following structural formula:



The vials contain sterile vancomycin hydrochloride equivalent to either 500 mg or 1 g vancomycin activity. Vancomycin hydrochloride is an off-white lyophilized plug. When reconstituted in water, it forms a clear solution with a pH range of 2.5 to 4.5. This product is oxygen sensitive.

CLINICAL PHARMACOLOGY

Vancomycin is poorly absorbed after oral administration; it is given intravenously for therapy of systemic infections. Intramuscular injection is painful.

In subjects with normal kidney function, multiple intravenous dosing of 1 g of vancomycin (15 mg/kg) infused over 60 minutes produces mean plasma concentrations of approximately 63 µg/mL immediately after the completion of infusion, mean plasma concentrations of approximately 23 µg/mL 2 hours after infusion, and mean plasma concentrations of approximately 8 µg/mL 11 hours after the end of the infusion. Multiple dosing of 500 mg infused over 30 minutes produces mean plasma concentrations of about 49 µg/mL at the completion of infusion, mean plasma concentrations of about 19 µg/mL 2 hours after infusion, and mean plasma concentrations of about 10 µg/mL 6 hours after infusion. The plasma concentrations during multiple dosing are similar to those after a single dose.

The mean elimination half-life of vancomycin from plasma is 4 to 6 hours in subjects with normal renal function. In the first 24 hours, about 75% of an administered dose of vancomycin is excreted in urine by glomerular filtration. Mean plasma clearance is about 0.058 L/kg/h, and mean renal clearance is about 0.048 L/kg/h. Renal dysfunction slows excretion of vancomycin. In anephric patients, the average half-life of elimination is 7.5 days. The distribution coefficient is from 0.3 to 0.43 L/kg. There is no apparent metabolism of the drug. About 60% of an intraperitoneal dose of vancomycin administered during peritoneal dialysis is absorbed systemically in 6 hours. Serum concentrations of about 10 µg/mL are achieved by intraperitoneal injection of 30 mg/kg of vancomycin. Although vancomycin is not effectively removed by either hemodialysis or peritoneal dialysis, there have been reports of increased vancomycin clearance with hemoperfusion and hemofiltration.

Total systemic and renal clearance of vancomycin may be reduced in the elderly.

Vancomycin is approximately 55% serum protein bound as measured by ultrafiltration at vancomycin serum concentrations of 10 to 100 µg/mL. After IV administration of Vancocin HCl, inhibitory concentrations are present in pleural, pericardial, ascitic, and synovial fluids; in urine; in peritoneal dialysis fluid; and in atrial appendage tissue. Vancocin HCl does not readily diffuse across normal meninges into the spinal fluid; but, when the meninges are inflamed, penetration into the spinal fluid occurs.

Microbiology--The bactericidal action of vancomycin results primarily from inhibition of cell-wall biosynthesis. In addition, vancomycin alters bacterial-cell-membrane permeability and RNA synthesis. There is no cross-resistance between vancomycin and other antibiotics. Vancomycin is active against staphylococci, including *Staphylococcus aureus* and *Staphylococcus epidermidis* (including heterogeneous methicillin-resistant strains); streptococci, including *Streptococcus pyogenes, Streptococcus pneumoniae* (including penicillin-resistant strains), *Streptococcus agalactiae,* the viridans group, *Streptococcus bovis,* and enterococci (eg, *Enterococcus faecalis* [formerly *Streptococcus faecalis*]); *Clostridium difficile* (eg, toxigenic strains implicated in pseudomembranous enterocolitis); and diphtheroids. Other organisms that are susceptible to vancomycin *in vitro* include *Listeria monocytogenes, Lactobacillus* species, *Actinomyces* species, *Clostridium* species, and *Bacillus* species.

In vitro resistance to vancomycin has been reported among some enterococcal and staphylococcal isolates.

Vancomycin is not active *in vitro* against gram-negative bacilli, mycobacteria, or fungi.

Synergy--The combination of vancomycin and an aminoglycoside acts synergistically *in vitro* against many strains of *S. aureus,* nonenterococcal group D streptococci, enterococci, and *Streptococcus* species (viridans group).

Disk Susceptibility Tests--The standardized disk method described by the National Committee for Clinical Laboratory Standards has been recommended to test susceptibility to vancomycin. Results of standard susceptibility tests with a 30-µg vancomycin hydrochloride disk should be interpreted according to the following criteria: Susceptible organisms produce zones greater than or equal to 12 mm, indicating that the test organism is likely to respond to therapy. Organisms that produce zones of 10 or 11 mm are considered to be of intermediate susceptibility. Organisms in this category are likely to respond if the infection is confined to tissues or fluids in which high antibiotic concentrations are attained. Resistant organisms produce zones of 9 mm or less, indicating that other therapy should be selected.

Using a standardized dilution method, a bacterial isolate may be considered susceptible if the MIC value for vancomycin is 4 µg/mL or less. Organisms are considered resistant to vancomycin if the MIC is greater than or equal to 16 µg/mL. Organisms having an MIC value of less than 16 µg/mL but greater than 4 µg/mL are considered to be of intermediate susceptibility.[1-2]

Standardized procedures require the use of laboratory control organisms. The 30-µg vancomycin disk should give zone diameters between 15 and 19 mm for *S. aureus* ATCC 25923. As with the standard diffusion methods, dilution procedures require the use of laboratory control organisms. Standard vancomycin powder should give MIC values in the range of 0.5 µg/mL to 2.0 µg/mL for *S. aureus* ATCC 29213. For *E. faecalis* ATCC 29212, the MIC range should be 1.0 to 4.0 µg/mL.

INDICATIONS AND USAGE

Vancocin HCl is indicated for the treatment of serious or severe infections caused by susceptible strains of methicillin-resistant (beta-lactam-resistant) staphylococci. It is indicated for penicillin-allergic patients, for patients who cannot receive or who have failed to respond to other drugs, including the penicillins or cephalosporins, and for infections caused by vancomycin-susceptible organisms that are resistant to other antimicrobial drugs. Vancocin HCl is indicated for initial therapy when methicillin-resistant staphylococci are suspected, but after susceptibility data are available, therapy should be adjusted accordingly.

Vancocin HCl is effective in the treatment of staphylococcal endocarditis. Its effectiveness has been documented in other infections due to staphylococci, including septicemia, bone infections, lower respiratory tract infections, and skin and skin structure infections. When staphylococcal infections are localized and purulent, antibiotics are used as adjuncts to appropriate surgical measures.

Vancocin HCl has been reported to be effective alone or in combination with an aminoglycoside for endocarditis caused by *Streptococcus viridans* or *S. bovis*. For endocarditis caused by enterococci (eg, *E. faecalis*), Vancocin HCl has been reported to be effective only in combination with an aminoglycoside.

Vancocin HCl has been reported to be effective for the treatment of diphtheroid endocarditis. Vancocin HCl has been used successfully in combination with either rifampin, an aminoglycoside, or both in early-onset prosthetic valve endocarditis caused by *S. epidermidis* or diphtheroids.

Specimens for bacteriologic cultures should be obtained in order to isolate and identify causative organisms and to determine their susceptibilities to Vancocin HCl.

The parenteral form of Vancocin HCl may be administered orally for treatment of antibiotic-associated pseudomembranous colitis caused by *C. difficile* and for staphylococcal enterocolitis. Parenteral administration of Vancocin HCl alone is of unproven benefit for these indications. **Vancocin HCl is not effective by the oral route for other types of infection.**

Although no controlled clinical efficacy studies have been conducted, intravenous vancomycin has been suggested by the American Heart Association and the American Dental Association as prophylaxis against bacterial endocarditis in penicillin-allergic patients who have congenital heart disease or rheumatic or other acquired valvular heart disease when these patients undergo dental procedures or surgical procedures of the upper respiratory tract.

Note: When selecting antibiotics for the prevention of bacterial endocarditis, the physician or dentist should read the full joint statement of the American Heart Association and the American Dental Association.[3]

CONTRAINDICATION

Vancocin HCl is contraindicated in patients with known hypersensitivity to this antibiotic.

WARNINGS

Rapid bolus administration (eg, over several minutes) may be associated with exaggerated hypotension, and, rarely, cardiac arrest.

Vancocin HCl should be administered in a dilute solution over a period of not less than 60 minutes to avoid rapid-infusion-related reactions. Stopping the infusion usually results in prompt cessation of these reactions.

Ototoxicity has occurred in patients receiving Vancocin HCl. It may be transient or permanent. It has been reported mostly in patients who have been given excessive doses, who have an underlying hearing loss, or who are receiving concomitant therapy with another ototoxic agent, such as an aminoglycoside. Vancomycin should be used with caution in patients with renal insufficiency because the risk of toxicity is appreciably increased by high, prolonged blood concentrations.

Dosage of Vancocin HCl must be adjusted for patients with renal dysfunction (*see* **PRECAUTIONS** *and* **DOSAGE AND ADMINISTRATION**).

Pseudomembranous colitis has been reported with nearly all antibacterial agents, including vancomycin, and may range in severity from mild to life-threatening. Therefore, it is important to consider this diagnosis in patients who present with diarrhea subsequent to the administration of antibacterial agents.

Treatment with antibacterial agents alters the normal flora of the colon and may permit overgrowth of clostridia. Studies indicate that a toxin produced by *Clostridium difficile* is a primary cause of "antibiotic-associated colitis." After the diagnosis of pseudomembranous colitis has been established, therapeutic measures should be initiated. Mild cases of pseudomembranous colitis usually respond to drug discontinuation alone. In moderate to severe cases, consideration should be given to management with fluids and electrolytes, protein supplementation, and treatment with an antibacterial drug clinically effective against *C. difficile* colitis.

PRECAUTIONS

General--Clinically significant serum concentrations have been reported in some patients who have taken multiple oral doses of vancomycin for active *C. difficile*-induced pseudomembranous colitis.

Prolonged use of Vancocin HCl may result in the overgrowth of nonsusceptible organisms. Careful observation of the patient is essential. If superinfection occurs during therapy, appropriate measures should be taken.

In order to minimize the risk of nephrotoxicity when treating patients with underlying renal dysfunction or patients receiving concomitant therapy with an aminoglycoside, serial monitoring of renal function should be performed and particular care should be taken in following appropriate dosing schedules (*see* **DOSAGE AND ADMINISTRATION**).

Serial tests of auditory function may be helpful in order to minimize the risk of ototoxicity.

Reversible neutropenia has been reported in patients receiving Vancocin HCl (*see* **ADVERSE REACTIONS**). Patients who will undergo prolonged therapy with Vancocin HCl or those who are receiving concomitant drugs that may cause neutropenia should have periodic monitoring of the leukocyte count.

Vancocin HCl is irritating to tissue and must be given by a secure intravenous route of administration. Pain, tenderness, and necrosis occur with intramuscular injection of Vancocin HCl or with inadvertent extravasation. Thrombophlebitis may occur, the frequency and severity of which can be minimized by administering the drug slowly as a dilute solution (2.5 to 5 g/L) and by rotating the sites of infusion.

There have been reports that the frequency of infusion-related events (including hypotension, flushing, erythema, urticaria, and pruritus) increases with the concomitant administration of anesthetic agents. Infusion-related events may be minimized by the administration of Vancocin HCl as a 60-minute infusion prior to anesthetic induction.

The safety and efficacy of vancomycin administration by the intrathecal (intralumbar or intraventricular) routes have not been assessed.

Reports have revealed that administration of sterile vancomycin HCl by the intraperitoneal route during continuous ambulatory peritoneal dialysis (CAPD) has resulted in a syndrome of chemical peritonitis. To date, this syndrome has ranged from a cloudy dialysate alone to a cloudy dialysate accompanied by variable degrees of abdominal pain and fever. This syndrome appears to be short-lived after discontinuation of intraperitoneal vancomycin.

Drug Interactions--Concomitant administration of vancomycin and anesthetic agents has been associated with erythema and histamine-like flushing (*see Usage in Pediatrics under* **PRECAUTIONS**) and anaphylactoid reactions (*see* **ADVERSE REACTIONS**).

Concurrent and/or sequential systemic or topical use of other potentially neurotoxic and/or nephrotoxic drugs, such as amphotericin B, aminoglycosides, bacitracin, polymyxin B, colistin, viomycin, or cisplatin, when indicated, requires careful monitoring.

Usage in Pregnancy--Pregnancy Category C--Animal reproduction studies have not been conducted with Vancocin HCl. It is not known whether Vancocin HCl can affect reproduction capacity. In a controlled clinical study, the potential ototoxic and nephrotoxic effects of Vancocin HCl on infants were evaluated when the drug was administered to pregnant women for serious staphylococcal infections complicating intravenous drug abuse. Vancocin HCl was found in cord blood. No sensorineural hearing loss or nephrotoxicity attributable to Vancocin HCl was noted. One infant whose mother

received Vancocin HCl in the third trimester experienced conductive hearing loss that was not attributed to the administration of Vancocin HCl. Because the number of patients treated in this study was limited and Vancocin HCl was administered only in the second and third trimesters, it is not known whether Vancocin HCl causes fetal harm. Vancocin HCl should be given to a pregnant woman only if clearly needed.

Nursing Mothers--Vancocin HCl is excreted in human milk. Caution should be exercised when Vancocin HCl is administered to a nursing woman. Because of the potential for adverse events, a decision should be made whether to discontinue nursing or to discontinue the drug, taking into account the importance of the drug to the mother.

Usage in Pediatrics--In premature neonates and young infants, it may be appropriate to confirm desired vancomycin serum concentrations. Concomitant administration of vancomycin and anesthetic agents has been associated with erythema and histamine-like flushing in children (*see* **ADVERSE REACTIONS**).

Geriatrics--The natural decrement of glomerular filtration with increasing age may lead to elevated vancomycin serum concentrations if dosage is not adjusted. Vancomycin dosage schedules should be adjusted in elderly patients (*see* **DOSAGE AND ADMINISTRATION**).

ADVERSE REACTIONS

Infusion-Related Events--During or soon after rapid infusion of Vancocin HCl, patients may develop anaphylactoid reactions, including hypotension (*see* **ANIMAL PHARMACOLOGY**), wheezing, dyspnea, urticaria, or pruritus. Rapid infusion may also cause flushing of the upper body ("Red Man Syndrome") or pain and muscle spasm of the chest and back. These reactions usually resolve within 20 minutes but may persist for several hours. Such events are infrequent if Vancocin HCl is given by a slow infusion over 60 minutes. In studies of normal volunteers, infusion-related events did not occur when Vancocin HCl was administered at a rate of 10 mg/min or less.

Nephrotoxicity--Rarely, renal failure, principally manifested by increased serum creatinine or BUN concentrations, especially in patients given large doses of Vancocin HCl, has been reported. Rare cases of interstitial nephritis have been reported. Most of these have occurred in patients who were given aminoglycosides concomitantly or who had preexisting kidney dysfunction. When Vancocin HCl was discontinued, azotemia resolved in most patients.

Gastrointestinal--Onset of pseudomembranous colitis symptoms may occur during or after antibiotic treatment (*see* **WARNINGS**).

Ototoxicity--A few dozen cases of hearing loss associated with Vancocin HCl have been reported. Most of these patients had kidney dysfunction or a preexisting hearing loss or were receiving concomitant treatment with an ototoxic drug. Vertigo, dizziness, and tinnitus have been reported rarely.

Hematopoietic--Reversible neutropenia, usually starting 1 week or more after onset of therapy with Vancocin HCl or after a total dosage of more than 25 g, has been reported for several dozen patients. Neutropenia appears to be promptly reversible when Vancocin HCl is discontinued. Thrombocytopenia has rarely been reported.

Although a causal relationship has not been established, reversible agranulocytosis (granulocytes $<500/mm^3$) has been reported rarely.

Phlebitis--Inflammation at the injection site has been reported.

Miscellaneous--Infrequently, patients have been reported to have had anaphylaxis, drug fever, nausea, chills, eosinophilia, rashes (including exfoliative dermatitis), linear IgA bullous dermatosis, Stevens-Johnson syndrome, toxic epidermal necrolysis, and rare cases of vasculitis in association with administration of Vancocin HCl.

Chemical peritonitis has been reported following intraperitoneal administration of vancomycin (*see* **PRECAUTIONS**).

OVERDOSAGE

Supportive care is advised, with maintenance of glomerular filtration. Vancomycin is poorly removed by dialysis. Hemofiltration and hemoperfusion with polysulfone resin have been reported to result in increased vancomycin clearance. The median lethal intravenous dose is 319 mg/kg in rats and 400 mg/kg in mice.

To obtain up-to-date information about the treatment of overdose, a good resource is your certified Regional Poison Control Center. Telephone numbers of certified poison control centers are listed in the *Physicians' Desk Reference (PDR)*. In managing overdosage, consider the possibility of multiple drug overdoses, interaction among drugs, and unusual drug kinetics in your patient.

DOSAGE AND ADMINISTRATION

Infusion-related events are related to both concentration and rate of administration of vancomycin. Concentrations of no more than 5 mg/mL and rates of no more than 10 mg/min are recommended in adults (see also age-specific recommendations). In selected patients in need of fluid restriction, a concentration up to 10 mg/mL may be used; use of such higher concentrations may increase the risk of infusion-related events. Infusion-related events may occur, however, at any rate or concentration.

Patients With Normal Renal Function

Adults--The usual daily intravenous dose is 2 g divided either as 500 mg every 6 hours or 1 g every 12 hours. Each dose should be administered at no more than 10 mg/min or over a period of at least 60 minutes, whichever is longer. Other patient factors, such as age or obesity, may call for modification of the usual intravenous daily dose.

Children--The usual intravenous dosage of Vancocin HCl is 10 mg/kg per dose given every 6 hours. Each dose should be administered over a period of at least 60 minutes.

Infants and Neonates--In neonates and young infants, the total daily intravenous dosage may be lower. In both neonates and infants, an initial dose of 15 mg/kg is suggested, followed by 10 mg/kg every 12 hours for neonates in the 1st week of life and every 8 hours thereafter up to the age of 1 month. Each dose should be administered over 60 minutes. Close monitoring of serum concentrations of vancomycin may be warranted in these patients.

Patients With Impaired Renal Function and Elderly Patients

Dosage adjustment must be made in patients with impaired renal function. In premature infants and the elderly, greater dosage reductions than expected may be necessary because of decreased renal function. Measurement of vancomycin serum concentrations can be helpful in optimizing therapy, especially in seriously ill patients with changing renal function. Vancomycin serum concentrations can be determined by use of microbiologic assay, radioimmunoassay, fluorescence polarization immunoassay, fluorescence immunoassay, or high-pressure liquid chromatography.

If creatinine clearance can be measured or estimated accurately, the dosage for most patients with renal impairment can be calculated using the following table. The dosage of Vancocin HCl per day in mg is about 15 times the glomerular filtration rate in mL/min:

DOSAGE TABLE FOR VANCOMYCIN
IN PATIENTS WITH IMPAIRED RENAL FUNCTION
(Adapted from Moellering et al)[4]

Creatinine Clearance mL/min	Vancomycin Dose mg/24 h
100	1,545
90	1,390
80	1,235
70	1,080
60	925
50	770
40	620
30	465
20	310
10	155

The initial dose should be no less than 15 mg/kg, even in patients with mild to moderate renal insufficiency.

The table is not valid for functionally anephric patients. For such patients, an initial dose of 15 mg/kg of body weight should be given to achieve prompt therapeutic serum concentrations. The dose required to maintain stable concentrations is 1.9 mg/kg/24 h. In patients with marked renal impairment, it may be more convenient to give maintenance doses of 250 to 1,000 mg once every several days rather than administering the drug on a daily basis. In anuria, a dose of 1,000 mg every 7 to 10 days has been recommended.

When only the serum creatinine concentration is known, the following formula (based on sex, weight, and age of the patient) may be used to calculate creatinine clearance. Calculated creatinine clearances (mL/min) are only estimates. The creatinine clearance should be measured promptly.

$$\text{Men:} \quad \frac{\text{Weight (kg)} \times (140 - \text{age in years})}{72 \times \text{serum creatinine concentration (mg/dL)}}$$

Women: 0.85 x above value

The serum creatinine must represent a steady state of renal function. Otherwise, the estimated value for creatinine clearance is not valid. Such a calculated clearance is an overestimate of actual clearance in patients with conditions: (1) characterized by decreasing renal function, such as shock, severe heart failure, or oliguria; (2) in which a normal relationship between muscle mass and total body weight is not present, such as obese patients or those with liver disease, edema, or ascites; and (3) accompanied by debilitation, malnutrition, or inactivity.

The safety and efficacy of vancomycin administration by the intrathecal (intralumbar or intraventricular) routes have not been assessed.

Intermittent infusion is the recommended method of administration.

PREPARATION AND STABILITY

At the time of use, reconstitute by adding either 10 mL of Sterile Water for Injection to the 500-mg vial or 20 mL of Sterile Water for Injection to the 1-g vial of dry, sterile vancomycin powder. Vials reconstituted in this manner will give a solution of 50 mg/mL. FURTHER DILUTION IS REQUIRED.

After reconstitution with Sterile Water for Injection, 5% Dextrose Injection, or 0.9% Sodium Chloride for Injection, the vials may be stored in a refrigerator for 14 days without significant loss of potency. Reconstituted solutions containing 500 mg of vancomycin must be diluted with at least 100 mL of diluent. Reconstituted solutions containing 1 g of vancomycin must be diluted with at least 200 mL of diluent. The desired dose, diluted in this manner, should be administered by intermittent intravenous infusion over a period of at least 60 minutes.

Compatibility With Intravenous Fluids--Solutions that are diluted with 5% Dextrose Injection or 0.9% Sodium Chloride Injection may be stored in a refrigerator for 14 days without significant loss of potency. Solutions that are diluted with the following infusion fluids may be stored in a refrigerator for 96 hours:

5% Dextrose Injection and 0.9% Sodium Chloride Injection, USP

Lactated Ringer's Injection, USP

Lactated Ringer's and 5% Dextrose Injection, USP

Normosol®-M and 5% Dextrose

Isolyte® E

Acetated Ringer's Injection

Vancomycin solution has a low pH that may cause chemical or physical instability when it is mixed with other compounds.

Mixtures of solutions of vancomycin and beta-lactam antibiotics have been shown to be physically incompatible. The likelihood of precipitation increases with higher concentrations of vancomycin. It is recommended to adequately flush the intravenous lines between the administration of these antibiotics. It is also recommended to dilute solutions of vancomycin to 5 mg/mL or less.

Although intravitreal injection is not an approved route of administration for vancomycin, precipitation has been reported after intravitreal injection of vancomycin and ceftazidime for endophthalmitis using different syringes and needles. The precipitates dissolved gradually, with complete clearing of the vitreous cavity over two months and with improvement of visual acuity.

Prior to administration, parenteral drug products should be inspected visually for particulate matter and discoloration whenever solution or container permits.

For Oral Administration--Oral Vancocin HCl is used in treating antibiotic-associated pseudomembranous colitis caused by *C. difficile* and for staphylococcal enterocolitis. Vancocin HCl is not effective by the oral route for other types of infections. The usual adult total daily dosage is 500 mg to 2 g given in 3 or 4 divided doses for 7 to 10 days. The total daily dosage in children is 40 mg/kg of body weight in 3 or 4 divided doses for 7 to 10 days. The total daily dosage should not exceed 2 g. The appropriate dose may be diluted in 1 oz of water and given to the patient to drink. Common flavoring syrups may

be added to the solution to improve the taste for oral administration. The diluted solution may be administered via a nasogastric tube.

HOW SUPPLIED

Vancocin® HCl Vials (or Sterile Vancomycin Hydrochloride, USP) are available in:
The 500 mg,* 10-mL vials are available as follows:

10-mL vials	NDC 0002-1444-01 (VL 657)
Traypak† of 25	NDC 0002-1444-25 (VL 657)

The 1 g,* 20-mL vials are available as follows:

Traypak of 25	NDC 0002-7321-25 (VL 7321)

Also available:
Vancocin HCl ADD-Vantage Vials (or Sterile Vancomycin Hydrochloride, USP) are available in:
The 500 mg,* 15-mL vials are available as follows:

Traypak of 10	NDC 0002-7297-10 (VL 7297)

The 1 g,* 15-mL vials are available as follows:

Traypak of 10	NDC 0002-7298-10 (VL 7298)

Vancocin HCl Pharmacy Bulk Package (or Vancomycin Hydrochloride for Injection, USP) is available in:
The 10 g,* 100-mL vials are available as follows:

100-mL vial	NDC 0002-7355-01 (VL 7355)

Prior to reconstitution, the vials may be stored at room temperature, 15° to 30°C (59° to 86°F).

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*Equivalent to vancomycin.
†Traypak™ (multivial carton, Lilly).

ANIMAL PHARMACOLOGY

In animal studies, hypotension and bradycardia occurred in dogs receiving an intravenous infusion of vancomycin hydrochloride, 25 mg/kg, at a concentration of 25 mg/mL and an infusion rate of 13.3 mL/min.

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Literature revised August 29, 2001

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